


REVIEW



The status of intensive care medicine research and a future agenda for very old patients in the ICU

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Abstract

The “very old intensive care patients” (abbreviated to VOPs; greater than 80 years old) are probably the fastest expanding subgroup of all intensive care unit (ICU) patients. Up until recently most ICU physicians have been reluctant to admit these VOPs. The general consensus was that there was little survival to gain and the incremental life expectancy of ICU admission was considered too small. Several publications have questioned this belief, but others have confirmed the poor long-term mortality rates in VOPs. More appropriate triage (resource limitation enforced decisions), admission decisions based on shared decision-making and improved prediction models are also needed for this particular patient group. Here, an expert panel proposes a research agenda for VOPs for the coming years.

Keywords: Octogenarians, Elderly, ICU, Mortality, Frailty, Severity of illness

What is the current standard of care for delivering the best possible critical care in this field?

Definition and epidemiology

A fundamental obstacle in the discussion of “elderly patients” is the lack of clear definitions for “elderly”, “old” or “very old” groups. When it comes to studies on the prognosis and prognostic factors of “elderly” patients this may be strongly influenced by the expected life expectancy in the population studied. In countries with high life expectancy, being “elderly” may translate into a greater benefit, compared with a population with a shorter life expectancy. It could, in fact, be more meaningful to define old age as expected life expectancy in the population of interest minus 10 years [1]. Despite the lack of a clear definition, the “very old intensive care unit patients” (VOPs) are a visibly expanding subgroup of intensive care unit (ICU) patients, which will continue to

grow. There are, however, not many large epidemiological studies available addressing this issue, and most, but not all, demonstrate an increasing proportion of elderly patients in the ICU population (Table 1).

In many countries the median age of the entire ICU population is already above 65 years as can be seen in the example in Fig. 1, and such patients are seen as routine. As a result, the focus has slowly shifted towards investigating the group above 75–80 years (the so-called very elderly intensive care patients, herein abbreviated VOPs), and this group will be the focus of this research agenda discussion.

Intensive care and post-ICU mortality increases with advancing age, a fact that has been acknowledged and incorporated in all severity of disease scoring systems. However, the group of VOPs in those studies is small and these patients differ in many ways not documented in traditional severity scores. In addition, many relevant outcome predictors in this patient population such as functional capacity and cognitive impairment are not incorporated into current severity of disease scores. It appears that it is not age per se but rather associated

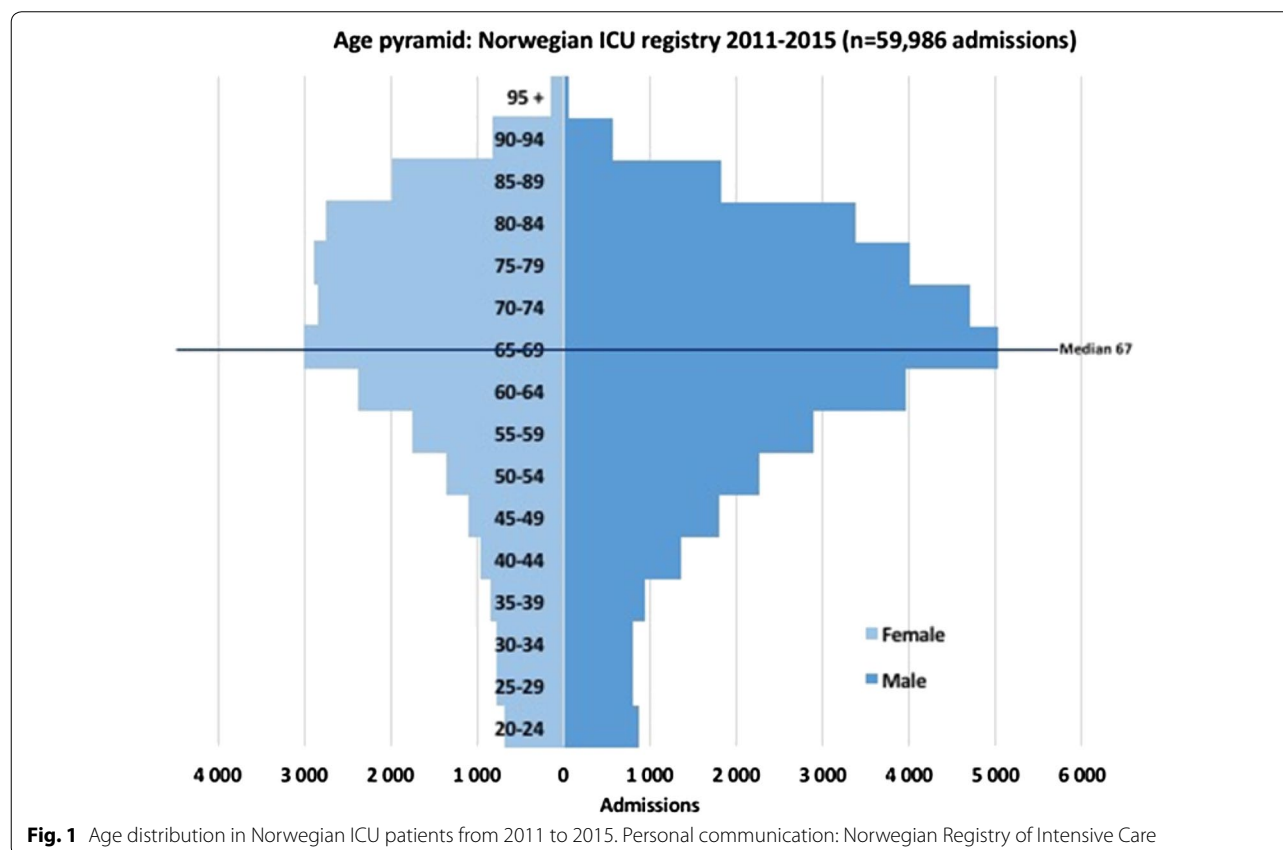
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Table 1 Proportion of VOPs in recent large epidemiological studies

Author	Country	Published	Number (≥ 80 years old)	Period	Results
Docherty [56]	Scotland	2016	3865	2005–2009	Decrease from 10% to 8.4%
Haas [57]	Netherlands	2015	39,558	2005–2014	Increase from 13.4% to 13.9%
Nielsson [58]	Denmark	2014	6266	2005–2011	Increase from 11.7% to 13.8%
Ihara [59]	Austria	2012	17,126	1998–2008	Increase from 11.5% to 15.3%
Bagshaw [6]	Australia and New Zealand	2009	15,640	2000–2005	Annual increase 5.6%

**Fig. 1** Age distribution in Norwegian ICU patients from 2011 to 2015. Personal communication: Norwegian Registry of Intensive Care

factors like severity of illness and premorbid functional status that contributed to the increased mortality [2].

Triage

Because of resource limitations in some places, certain patient groups are subjected to strict triage before admittance to the ICU. These may include VOPs, those with chronic diseases or active malignant diseases. In the large Eldicus study the elderly patients (greater than 75 years old) were found to have more ICU rejections than younger ones (less than 75 years old) despite having a greater mortality benefit [3]. On the other hand, in a prospective French study, no survival benefit was found in VOPs who were admitted versus rejected patients [4]. The imminent increase in the number of VOPs will

likely increase the need for triage even further as it seems unlikely there will be a significant growth of ICU bed numbers in Europe. Because triage is based on patient benefit, decisions require an assessment of prognosis. In the very elderly, triage decisions should change from being based on prognosis determined by acute physiology and co-morbidity to a more functional approach (See severity of disease models and the elderly).

ICU interventions and length of stay

Today, VOPs are not given the same amount of intensive care as their younger counterparts and it seems that the adage less is more has been practised in this group for a long time, likely with the intention not to inflict more harm than good on these patients. The literature

documents that organ support is lower and shorter in elderly compared to matched younger patients [5]. Median ICU length of stay (LOS), excluding elective post-operative admissions, is limited to 2–6 days for VOPs [6–8]. According to data from the Norwegian Intensive Care Registry from 2006 to 2009, significantly fewer VOPs were given ventilator support (40 vs 56%), and the median time on the mechanical ventilator (MV) and LOS on the ICU were shorter [9]. In a Scandinavian study of 53,305 ICU admissions, the median time to death was found to be 1.0 days in VOPs, compared to 1.7 days in patients 40–80 years old [9].

The lower workload and LOS in VOP are somewhat contradictory to the fact that physiological reserve is impaired in the elderly, suggesting that weaning from MV, renal replacement therapy (RRT) or vasopressors should be more difficult and thus duration of organ support and LOS should be longer. This suggests more proactive end-of-life (EOL) decision policy for elderly patients. However, over time an increase in the intensity of treatment in VOPs has been documented and associated with a mortality improvement after adjustment for severity [10].

Mortality

The 1-year overall mortality of VOPs varied from 40 to 70% in 11 different studies (see Fig. 2) [5].

In a group of ICU patients with circulatory shock the mortality was increased in old (75–85 years) and very old

(85+ years). In the latter group 97% had died after 1 year [11]. Also in the presence of acute kidney injury (AKI) most studies have documented that advanced age is independently associated with increase hospital mortality [12]. Mechanical ventilation, both invasive and non-invasive, is also associated with increased mortality in the elderly compared with younger age groups [13, 14]. Studies of sepsis have shown an exponential increase in the population-based incidence of sepsis with age, followed closely by an increased mortality. In a small study of septic shock in advanced age, major molecular pathways were found to be deregulated following severe infection, indicating that the systemic inflammatory response differs according to age [15].

Pre-ICU factors

Biological age does not necessarily parallel chronological age and is more difficult to estimate. Therefore, the focus is gradually shifting from traditional co-morbidity measures to the concept of frailty as an important marker of biological age and a predictor of outcome. As a concept frailty is relatively new to intensive care and is often defined as a clinical state of increased susceptibility from age-associated decline in reserve and function in a wide range of physiological systems [16]. Although frailty is associated with increased age, not all elderly are frail! Indeed, a relatively simplistic frailty score correlates strongly with mortality, incidence disability and quality of life (QOL) after ICU discharge [2].

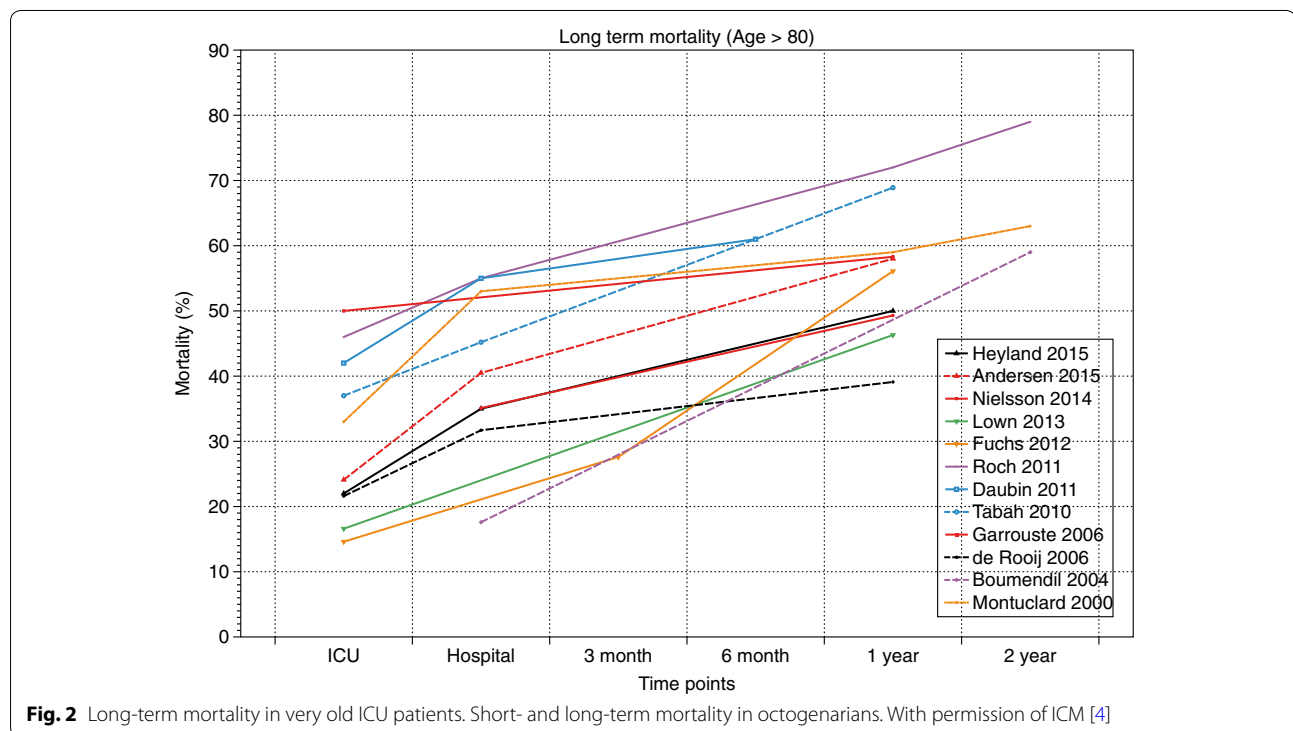


Fig. 2 Long-term mortality in very old ICU patients. Short- and long-term mortality in octogenarians. With permission of ICM [4]

Organisation

Today, most VOPs are treated in general ICUs (or organ-specific ICUs) and are most often treated by intensivists in typical cooperation with referring physicians. However, specific geriatric ICUs are scarce [17], and most VOPs are never visited by a geriatrician. Geriatricians' involvement is an advantage that recently has been found to provide a survival benefit in many other groups [18]. This benefit may reflect the more holistic approach a geriatrician may have to the VOP, leading to better decision-making. To include a geriatrician in shared decision-making may lead to better triage decisions as well. The increasing demand for ICU admission in the very old may be anticipated to increase future care costs. The development of options to limit costs may include the use of specialized intermediate care or step-down units, with geriatrician support, to treat VOPs in the future.

What have been the major recent advances in the field?

Admission bias

Despite apparently increasing numbers of VOPs potentially presenting for admission, physicians are often reluctant to admit them into the ICU. In an observational study of 2646 patients aged at least 80 years who met at least one ICU admission criterion at the emergency department (ED) visit, only 25% were referred for ICU admission and 12.4% were actually admitted [19]. Among refused patients, 1981 were not admitted because they were considered either too well or too sick by ED physicians and intensivists. Hospital mortality was 8.2% for the too well patients, 32.7% for those admitted to the ICU and 68.2% for those too sick. Interestingly, 6 months after referral, patients considered too well for ICU admission had a mortality rate (40.6%) approaching those admitted to the ICU (47.5%) [20]. A decision to admit an elderly patient to ICU with initial full code treatment (no restriction) does not preclude secondary decision to withdraw or withhold treatment. As a matter of fact a liberal admission policy is sustainable only if the patient condition is reassessed a few days after admission. At that time assessment of response to treatment is available together with information that is usually lacking at the time of admission (patient and family wishes, medical history, GP information, etc.).

Delirium

VOPs are more prone to neuropsychological complications such as delirium than their younger counterparts. A lot of confounders present in the elderly can create a predisposition for delirium and include impaired vision, hearing as well as other sensory deficits. Up to 50% of critically ill patients may develop delirium, the incidence of which increases with age [21]. As a result delirium adds

to the burden of poor outcomes in VOPs. In a single-centre study, it was shown that haloperidol prophylaxis in critically ill patients with high risk of delirium resulted in a lower delirium incidence. This effect was most pronounced in very high risk patients. A multicentre study on that strategy has just been completed and is awaiting final analyses [22]. Experiences from perioperative care in VOPs also suggest that preoperative prophylaxis with haloperidol [23] and recently with dexmedetomidine [24] also may be effective.

In the elderly, non-pharmacologic approaches to reduce the burden of delirium include mobilisation and help with issues related to vision (glasses) and hearing (hearing aids).

Long-term sequelae

Survivors of critical illness have been found to suffer from long-term sequelae, including increased long-term mortality [25], poor quality-adjusted survival [26], cognitive impairment and functional disability [27, 28]. VOPs are not exempt from such adverse events, which often are perceived to occur beyond the scope of intensive care. However, VOPs may follow a number of trajectories that may be influenced by the care in the ICU. For example, a negative trajectory may result from heavy sedation, prolonged ventilation, immobilisation, lack of nutrients etc. The VOP cohort is probably the most vulnerable for functional decline. In a prospective cohort study in the ED, 2646 patients over 80 years old potentially qualified for ICU admission [20]. Among the 1230 patients who were alive 6 months after the ED visit, 1085 (88%) had their functional status evaluated. Only one-third were independent for all activities listed in Katz's scale, while 16.2% were unable to perform at least one activity that they had been able to perform at the time of the ED visit. In the subgroup of patients that had been admitted to the ICU, 12% experienced a minimum of one point loss in at least one dimension of the activities of daily living in comparison to baseline. Therefore, in both groups, 6 months after the ED visit, 63% of patients had either died or experienced functional deterioration. Moreover, a recent Canadian cohort study of 610 VOPs with ICU length of stay of more than 24 h reported significantly worse physical functioning after 3, 6 and 12 months compared with age- and gender-matched controls [29]. In a single-centre study, Hofhuis et al. document an improvement in health-related QOL over time in 49 VOPs with 6-month follow-up [30]. This encouraging result is, however, not a consistent finding, and has been contradicted by other studies. For example, cognitive and functional impairment among survivors of severe sepsis had not improved after 1, 3 and 5 years in the study by Iwashyna et al. [28]. In the study by Griffith et al. [31], the physical component

of SF36 was similar in patients below and above 64 years old, and it did not improve from 6 to 12 months after discharge. The mental score was better preserved in the patients over 64 years old but again did not improve over time. In the study by Kaarlola et al. [32], QOL was lower for the very elderly patients, although 97% of the elderly survivors lived at home and 88% of them considered their QOL satisfactory or good after hospital discharge.

The high refusal rates of ICUs of very elderly patients has allowed comparison of the incremental benefit of ICU admission in VOPs [33, 34]. As already discussed, there is a short-term mortality benefit of ICU admission of VOPs [3, 32]. However, 1-year mortality appears equally poor in both admitted and refused very elderly patients [33]. Moreover, when reductions in function and QOL were considered, the long-term benefits are even less substantial [34]. Although long-term QOL may appear relatively poor it does appear to be similar to age-matched populations [33, 34]. It is quite revealing to consider outcomes in terms of quality-adjusted life years (QALYs). Kaarlola et al. showed that the QALYs derived from ICU admission of patients over 80 years old would be a median of 4.1 years, in the 65–79 years old group it would be 10.2 years and in patients less than 65 years old it would be 22 years [32].

Factors associated with mortality

Being able to predict which VOP is going to benefit from ICU admission and will have a long-term survival in good QOL is of the utmost importance. In general ICU patients, severity of illness, socio-economic status, co-morbidities, frailty at admission and treatment limitations (e.g. “do not resuscitate” orders) are associated with outcome. In VOPs, the functional status and frailty before admission appear to be more important than the severity of illness [35]. Interestingly, even in VOPs, age remains an independent risk factor for poor outcome. In a secondary analysis of 6205 patients with community-acquired pneumonia (CAP), 508 (8.2%) died within 30 days. In the overall population, mortality increased with age; however, in the subgroup of patients with one co-morbidity or less, mortality was not different between patients younger than 65 years old and those 65–79 years old, but it was higher for those aged 80 years and older, suggesting that age greater than 80 years, instead of age greater than 65 years, should be considered as the appropriate age-related risk factor for poor outcome in CAP [36].

What are the common beliefs that have been contradicted by recent trials?

Patients’ wishes and directives

It is good practice to establish a patient’s wishes at the start of their treatment and during the ICU stay. This is

particularly relevant during treatment when increasing degrees of intervention are desired, especially in patients approaching EOL. Earlier studies have revealed a deficiency in establishing patient wishes in real life. Subsequently much effort has gone into promoting the need for treating physicians to acquire knowledge of a patient’s wishes to establish goals of care prior to and during ICU care. Although it is widely believed that this practice is universal, several studies in VOPs directly oppose this. A recent French study in competent VOPs reported that only 13% had been asked about their treatment preferences and willingness to be admitted to the ICU prior to ICU admission [37]. Data from the North American SUPPORT and European Ethicus studies also documented that information about a patient’s wishes regarding EOL decisions was available in only 20% of competent patients [38, 39]. This was, again, confirmed in more recent studies [40, 41], in which only 57% of families were involved in providing information related to EOL decisions in VOPs. A recent Asian study of elderly (mean greater than 80 years old) patients in ICU similarly reported that pre-acute event advance directives were documented in less than 3% of reviewed cases in ICU [42]. While several studies do document patient and family participation in “shared decision-making” it is clear that much work is required to ensure that patients’ wishes are systematically sought after in elderly patients, especially as available evidence indicates that up to 50% of VOPs would prefer care of lower intensity and focused primarily on comfort [19, 43].

Costs–benefits for elderly patients

Selection of patients for ICU admission is dependent on assessment of the cost–benefit ratio. In areas with unlimited resources this balance is predominantly determined by a cost–benefit analysis which is based on individual patient preferences. However, when resources are limited, individuals who are more likely to benefit from ICU admission are preferred above those with a lower likelihood of benefit (distributive justice principle). If we want to be able to make objective decisions regarding the cost of ICU care, in both human suffering and monetary terms, we must know (or estimate) the chance of health benefit. Vice versa, the outcome of non-ICU care must also be known if we want to make the proper comparison. As discussed, there is ample evidence that age is associated with decisions to refuse ICU admission [36–39]. Yet, there currently is no robust or validated clinical prediction tool that is able to reliably indicate the VOP who will substantially benefit from ICU care. Evidently, survival chances of VOPs are highly variable [6, 20, 44]. Substantially more data is required to be able to answer these questions if we want to improve the consistency

and accuracy of admission decisions concerning VOPs. There are some studies looking at cost-effectiveness and cost-utility ratio in ICU and documenting higher ratios for elderly patients. This is expected since the mortality is higher and the life expectancy shorter for elderly patients compared to younger patients [45].

What are remaining areas of uncertainty?

Insufficient epidemiological data

Almost all countries are faced with ageing populations; therefore, it is important to fill the large knowledge gaps currently present. Epidemiological studies reporting data on critical illness in the very old are limited to a few geographical regions. In Europe most studies come from France, the Netherlands and the Nordic countries, whereas studies from the Eastern Europe are scarce. In the rest of the world studies most frequently come from Canada, the USA and Australia/New Zealand. This fact may also distort the “signal” given regarding the outcome of VOP, and may reflect a higher organisational status and logistics towards a higher level of care, also with regards to VOP.

Effects on country level

Some estimates demand an increase in ICU bed numbers of 50% to cope with an ageing population [46]. In line with this increase will be an increased demand for specific rehabilitation programs and beds in residential homes or nursing homes, which also will increase global health costs. Very few countries will be capable of supporting an adequate expansion of services since financial resources are increasingly limited. The availability of health care personnel will also pose a problem with shrinking younger workforce availability. Hence, greater attention to advance care planning in primary care and more aggressive pre-ICU triage both appear inevitable in the future.

Severity of disease models and the elderly

Over recent years we have learned a lot about the prognostic determinants of the elderly patient, both in terms of morbidity and mortality. The impact of age and pre-existing co-morbid diseases in the most recent severity of illness scoring systems has been increasing and is now close to 50% [47]. However, many studies continue to use the same variables that were used when the previous severity of illness models were developed [48, 49]. This has led to decreased discrimination of these models in the advanced age groups (see Fig. 3). In all contemporary severity of illness systems, the very old only contribute a minor proportion of the study population, which may explain why important variables related to old age, like dementia, mobility, activities of daily living and general

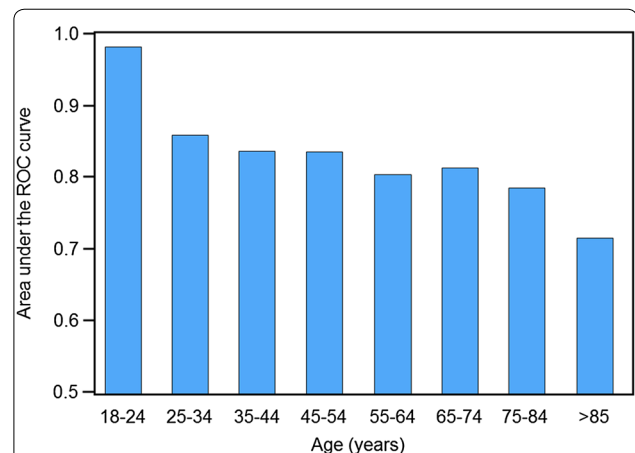


Fig. 3 Decreasing discrimination of severity of illness score (SAPS II) with increasing age groups. Unpublished data from the EURICUS-1 study regarding SAPS II [48]

Table 2 Mean age of included patients in published severity scores

Severity score	Mean age	Year of publication
Apache II	Patients >65 years: 24–54%	1985
SAPS II	57.2	1993
APACHE II in UK	56.3	1993
MPM II	Survivors 55.4; non survivors 62.9	1993
APACHE III	59.6	1991
SAPS II revisited	57.3	2005
SAPS III	60.7	2005
APACHE IV	61.5	2006
CUB-REA network*	52.4	1993
CUB-REA network	57.4	2005
CUB-REA network	62.6	2014

* Data derived from CUB-REA network, which includes more than 30 ICUs in the Paris area

measures of frailty, are excluded (see Table 2). As the number of patients within this currently small group is increasing, developing scoring systems sensitive to prognosis within this group is a priority.

Although cumbersome, it is becoming increasingly justified to incorporate a frailty measure into prediction models in order to adjust for the influence of physiological age rather than biological age. The optimal frailty tool, what weighting allocation, and inclusion as an independent variable, or an effect modifier on physiological variables, has yet to be determined. Currently several different tools to assess frailty exist. Some are rapid screening or case-finding tools (i.e. global subjective assessments like clinical frailty score, or simple performance measures

Table 3 Ten potential trials recommended by the expert panel

1. The occurrence of pre- and post-ICU admission frailty and sarcopenia and its effects of functional outcomes
Frailty and sarcopenia are probably very important to understand outcomes in the very old ICU patients. This condition has, for a long time, been in focus among geriatricians but has only recently gained interest in the ICU community [2]. It is of interest to study how rapid screens for frailty using objective muscular assessment could predict frailty and response to ICU support and outcome. This multicentre study should define the link between frailty and sarcopenia in this population and its effect on 3-month mortality and ability to regain pre-ICU functional status
2. What is the opinion of octogenarians towards use of critical care resources in acute, severe vital organ failure? A European survey among 10,000 octogenarians
In the end, the attitude in any individual patient with regards to ICU admission is the most important piece of information the ICU team needs. This is particularly important in octogenarians that, regardless of pre-ICU status, have a comparably shorter expected lifetime. This study should highlight the opinion of octogenarians throughout Europe to five preselected imagined ICU scenarios, and their opinion to ICU treatment if the case should be a reality in their own life
3. The effects of including a geriatrician in the early assessment and discharge of octogenarians. A prospective randomised trial (RCT)
Inclusion of geriatric consultancy has proven valuable in other areas of medicine [17]. Only occasionally geriatricians are included in the care of ICU patients. This might be of particularly great value in ICU survivors at discharge from the unit. This prospective RCT will study the value of inclusion of a geriatrician in the evaluation of octogenarians before discharge to ward. The primary aim of the study is recovery of pre-ICU health status in the two groups at 3 and 12 months
4. The effects of non-pharmacological interventions to reduce delirium in the ICU. An open randomised prospective trial
Delirium is of particular concern in elderly ICU patients since its prevalence is increasing with age and it is a marker of poor outcomes. There are few therapeutic options as soon as delirium is established, so prevention is paramount. In this study non-pharmacologic interventions like minimal sedation, early mobilisation and stimulation with light and sounds will be given in an open randomised multicentre study. Delirium occurrence and duration are expected to be reduced in the treatment arm
5. The burden of intensive care, a prospective study in caregivers of octogenarians in the ICU
More than half of patients with ventilator support surviving critical care require caregiver assistance after ICU discharge [52]. Many caregivers report high levels of PTSD and depressive symptoms [53]. Variables significantly associated with worse mental health outcomes in caregivers are age and less social support. These findings are even more relevant in the very old surviving an ICU stay especially when they overlap with dementia, frailty and sarcopenia. This study will identify the physical, psychological and socio-economic burden of caregivers of octogenarians surviving an ICU admission along with their predictors
6. Development of a prognostic tool for the very old ICU patients
Traditional prognostic severity scoring systems often fail to give an accurate estimation of subgroup survival. There have been attempts to develop alternatives but rather than using traditional acute physiological derangements many believe pre-ICU items such as frailty, sarcopenia and cognition will be more important determinants of outcome. This will be tested in ICU patients ≥ 80 years using a number of pre-ICU factors with some key factors present at admission
7. Sepsis in the very old ICU patients: incidence and outcomes
Available epidemiological data demonstrates an exponential increase in the incidence of sepsis and also mortality in the elderly ICU patients. Using the new sepsis definition, a large prospective cohort study of sepsis in the elderly patients will define prognostic factors for survival with particular focus on the development of single and multi-organ failure in this cohort. The study will guide clinicians on the basis of an organ dysfunction map using the SOFA score
8. Dementia development after ICU discharge of octogenarians. A prospective follow-up study
The development of cognitive impairment after an ICU stay is linked to the occurrence and duration of delirium during the critical illness [54, 55]. Delirium has been shown to worsen a pre-existing dementia in non-critically ill patients. This longitudinal cohort study will further characterize the occurrence of dementia, the type of dementia based on neuropsychological, neuroimaging and laboratory evaluations, and the identification of other potential risk factors
9. Pharmacokinetics of midazolam, propofol and dexmedetomidine in very old ICU patients
The pharmacokinetics and pharmacodynamics of common sedatives used in the ICU are only partially studied in elderly with organ dysfunction. This study will clarify distribution volume, biological half-life and elimination pathways in this group. This study may give clinicians more information on correct dosing of these medications in elderly ICU patients
10. End of life trajectories in the very old. A European multicentre study
The increase in life expectancy has led to a higher utilisation of intensive treatments for older patients even in patients with dementia. It is, however, still unclear if there might be a risk of overtreatment or undertreatment of older patients in the setting of a critical illness. This multicentre study will provide the characterization of older patients and the identification of end of life trajectories providing clinicians with predictor tools including specific multidimensional geriatric evaluation to support the daily clinical decisions

like gait speed), whereas others are more comprehensive multi-domain tools that can focus attention on the specific domains or components that are contributing to frailty (i.e. physical, functional, cognitive, mobility, emotional, social, nutritional, sarcopenia etc.). The current gold standard for frailty diagnosis, which is a comprehensive geriatric assessment (CGA) is complex. Hence, further exploration to develop a generally accepted tiered

evaluation of patients at the bedside as well as a simple tool integration into risk models is needed.

A predictive scoring model was constructed on the basis of data that is readily available within 24 h after admission: gender, stroke, severity of illness, co-morbidity and frailty. This model accurately predicted survival and functional performance [50]. Another simple predictive scoring tool has been published. This model

appeared useful to guide triage decisions prior to ICU admission of VOPs [51]. While both have potential, neither scoring system has been clinically or externally evaluated.

There is always the question whether a scoring system will ever have sufficient discrimination to prove valuable in individual decision-making in VOPs. Nevertheless, multidisciplinary decision-making integrating objective elements, which probably is used by many ICUs today, will still play an important role in these difficult tasks.

What is the attitude of the elderly and their family?

There is insufficient knowledge of what the very old population wish to be done if they become critically ill. This applies to topics like cardiopulmonary resuscitation (CPR) and organ support versus comfort and care. Probably very few elderly, their families and society at large have a realistic insight into what intensive care really means and that mortality and morbidity are so much higher than in their younger counterparts. Obviously, this is influenced by cultural, religious and judicial factors, and many of these factors are country specific.

Burden of caregivers

Finally, the family and other caregivers around VOPs are exposed to the burden of critical illness. Many suffer from this insult in their own ways [52, 53]. This might be particularly true in the family members of the elderly ICU survivors, but little is known about the post-ICU syndrome in these family members nor of its consequences in the long run.

What the international group of experts recommend as the top 10 studies/trials to be done in the next 10 years: what are the expected outcomes/results of these trials?

After an internal voting process (using SurveyMonkey) the group decided to recommend ten potential trials outlined in Table 3. In most of these studies there should, whenever possible, be a comparison group of less old ICU patients in order to highlight specific age-dependent differences in old and very old ICU patients.

Conclusions

This paper reviews the literature and challenges some long-held beliefs in the treatment of “very elderly intensive care patients” (VOPs). Short-term survival may clearly benefit from ICU treatment but 1-year mortality is very high. There are indications that the incremental mortality benefit of very old patients admitted to the ICU is not substantial [4]. If other important outcomes are considered (functional outcome and quality of life) the beneficial outcome from intensive care therapy is even less certain. As more and more very elderly patients

are entering our health care systems, pre-admission goal of care discussions, advance directive availability and the triage of VOPs need to be improved. Several gaps of knowledge have been identified (see Table 3), and whenever appropriate, data from the very old should be distinguished from that of younger age groups.

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Compliance with ethical standards

Conflicts of interest

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References

1. Scherbov S, Sanderson WC (2016) New approaches to the conceptualization and measurement of age and aging. *J Aging Health* 28:1159–1177. doi:10.1177/0898264316656517
2. Bagshaw SM, Stelfox HT, Johnson JA, McDermid RC, Rolfson DB, Tsuyuki RT, Ibrahim Q, Majumdar SR (2015) Long-term association between frailty and health-related quality of life among survivors of critical illness: a prospective multicenter cohort study. *Crit Care Med* 43:973–982. doi:10.1097/CCM.0000000000000860
3. Sprung CL, Artigas A, Kesecioglu J, Pezzi A, Wiis J, Pirracchio R et al (2012) The Eldicus prospective, observational study of triage decision making in European intensive care units. Part II: intensive care benefit for the elderly. *Crit Care Med* 40:132–138. doi:10.1097/CCM.0b013e318232d6b0
4. Boumendil A, Latouche A, Guidet B, ICE-CUB Study Group (2011) On the benefit of intensive care for very old patients. *Arch Intern Med* 171:1116–1117. doi:10.1001/archinternmed.2011.102
5. Boumendil A, Aegerter P, Guidet B, CUB-Rea Network (2005) Treatment intensity and outcome of patients aged 80 and older in intensive care units: a multicenter matched-cohort study. *J Am Geriatr Soc* 53:88–93. doi:10.1111/j.1532-5415.2005.53016.x
6. Bagshaw SM, Webb SA, Delaney A, George C, Pilcher D, Hart GK, Bellomo R (2009) Very old patients admitted to intensive care in Australia and New

- Zealand: a multi-centre cohort analysis. *Crit Care* 13(2):R45. doi:[10.1186/cc7768](https://doi.org/10.1186/cc7768)
7. Heyland D, Cook D, Bagshaw SM, Garland A, Stelfox HT, Mehta S, Dodek P, Kutsogiannis J, Burns K, Muscedere J, Turgeon AF, Fowler R, Jiang X, Day AG, Canadian Critical Care Trials Group, Canadian Researchers at the End of Life Network (2015) The very elderly admitted to ICU: a quality finish? *Crit Care Med* 43:1352–1360. doi:[10.1097/CCM.0000000000001024](https://doi.org/10.1097/CCM.0000000000001024)
8. Boumendil A, Maury E, Reinhard I, Luquel L, Offenstadt G, Guidet B (2004) Prognosis of patients aged 80 years and over admitted in medical intensive care unit. *Intensive Care Med* 30:647–654. doi:[10.1007/s00134-003-2150-z](https://doi.org/10.1007/s00134-003-2150-z)
9. Andersen FH, Kvåle R (2012) Do elderly intensive care unit patients receive less intensive care treatment and have higher mortality? *Acta Anaesthesiol Scand* 56:1298–1305. doi:[10.1111/j.1399-6576.2012.02782.x](https://doi.org/10.1111/j.1399-6576.2012.02782.x)
10. Lerolle N, Trinquart L, Bornstein C, Tadié J-M, Imbert A, Diehl J-L et al (2010) Increased intensity of treatment and decreased mortality in elderly patients in an intensive care unit over a decade. *Crit Care Med* 38:59–64. doi:[10.1097/CCM.0b013e3181b088ec](https://doi.org/10.1097/CCM.0b013e3181b088ec)
11. Biston P, Aldecoa C, Devriendt J, Madl C, Chochrad D, Vincent J-L et al (2014) Outcome of elderly patients with circulatory failure. *Intensive Care Med* 40:50–56. doi:[10.1007/s00134-013-3121-7](https://doi.org/10.1007/s00134-013-3121-7)
12. Chronopoulos A, Rosner MH, Cruz DN, Ronco C (2010) Acute kidney injury in elderly intensive care patients: a review. *Intensive Care Med* 36:1454–1464. doi:[10.1007/s00134-010-1957-7](https://doi.org/10.1007/s00134-010-1957-7)
13. Schortgen F, Follin A, Piccari L, Roche-Campo F, Carteaux G, Taillandier-Herich E et al (2012) Results of noninvasive ventilation in very old patients. *Ann Intensive Care* 21:5. doi:[10.1186/2110-5820-2-5](https://doi.org/10.1186/2110-5820-2-5)
14. Esteban A, Anzueto A, Frutos-Vivar F, Alía I, Ely EW, Brochard L et al (2004) Outcome of older patients receiving mechanical ventilation. *Intensive Care Med* 30:639–646. doi:[10.1016/j.cger.2010.08.009](https://doi.org/10.1016/j.cger.2010.08.009)
15. da Silva Vieira, Pellegrina D, Severino P, Vieira Barbeiro H, Maziero Andreghetto F, Tadeu Velasco I, Possolo de Souza H et al (2015) Septic shock in advanced age: transcriptome analysis reveals altered molecular signatures in neutrophil granulocytes. *PLoS One* 10(6):e0128341. doi:[10.1371/journal.pone.0128341](https://doi.org/10.1371/journal.pone.0128341)
16. Xue Qian-Li (2011) The frailty syndrome: definition and natural history. *Clin Geriatr Med* 27(1):1–15. doi:[10.1016/j.cger.2010.08.009](https://doi.org/10.1016/j.cger.2010.08.009)
17. Zeng A, Song X, Dong J, Mitnitski A, Liu J, Guo Z et al (2015) Mortality in relation to frailty in patients admitted to a specialized geriatric intensive care unit. *J Gerontol A Biol Sci Med Sci* 70:1586–1594. doi:[10.1093/gerona/glv084](https://doi.org/10.1093/gerona/glv084)
18. Boddaert J, Cohen-Bittan J, Khiami F, Le Manach Y, Raux M, Beinis J-Y et al (2014) Postoperative admission to a dedicated geriatric unit decreases mortality in elderly patients with hip fracture. *PLoS One* 9(1):e83795. doi:[10.1371/journal.pone.0083795](https://doi.org/10.1371/journal.pone.0083795)
19. Garrouste-Orgeas M, Boumendil A, Pateron D, Aegerter P, Somme D, Simon T, Guidet B (2009) Selection of intensive care unit admission criteria for patients aged 80 years and over and compliance of emergency and intensive care unit physicians with the selected criteria: an observational, multicenter, prospective study. *Crit Care Med* 37:2919–2928. doi:[10.1097/CCM.0b013e3181b019f0](https://doi.org/10.1097/CCM.0b013e3181b019f0)
20. Boumendil A, Angus DC, Guitonneau AL, Menn AM, Ginsburg C, Takun K et al (2012) Variability of intensive care admission decisions for the very elderly. *PLoS One* 7(4):e34387. doi:[10.1371/journal.pone.0034387](https://doi.org/10.1371/journal.pone.0034387)
21. Zaai IJ, Devlin JW, Peelen LM, Slooter AJC (2015) A systematic review of risk factors for delirium in the ICU. *Crit Care Med* 43:40–47. doi:[10.1097/CCM.0000000000000625](https://doi.org/10.1097/CCM.0000000000000625)
22. van den Boogaard M, Schoohoven L, van Achterberg T, van den Hoeven JG, Pickkers P (2013) Haloperidol prophylaxis in critically ill patients with a high risk of delirium. *Crit Care* 17:R9. doi:[10.1186/cc11933](https://doi.org/10.1186/cc11933)
23. Kalisvaart KJ, De Jonghe JF, Bogaards MJ, Vreeswijk R, Egberts TCG, Burger BJ et al (2005) Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study. *J Am Geriatr Soc* 53(10):1658–1666. doi:[10.1111/j.1532-5415.2005.53503.x](https://doi.org/10.1111/j.1532-5415.2005.53503.x)
24. Su X, Meng ZT, Wu XH, Cui F, Li HL, Wang DX et al (2016) Dexmedetomidine for prevention of delirium in elderly patients after non-cardiac surgery: a randomised, double-blind, placebo-controlled trial. *Lancet* 388(10158):1893–1902. doi:[10.1016/S0140-6736\(16\)30580-3](https://doi.org/10.1016/S0140-6736(16)30580-3)
25. Kaplan V, Clermont G, Griffin MF, Kasal J, Watson RS, Linde-Zwirble WT, Angus DC (2003) Pneumonia: still the old man's friend? *Arch Intern Med* 163:317–323
26. Angus DC, Musthafa AA, Clermont G, Griffin MF, Linde-Zwirble WT, Dremsizov TT, Pinsky MR (2001) Quality-adjusted survival in the first year after the acute respiratory distress syndrome. *Am J Respir Crit Care Med* 163:1389–1394. doi:[10.1164/ajrccm.163.6.2005123](https://doi.org/10.1164/ajrccm.163.6.2005123)
27. Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, Brummel NE, Hughes CG, Vasilevskis EE, Shintani AK, Moons KG, Geevarghese SK, Canonico A, Hopkins RO, Bernard GR, Dittus RS, Ely EW, The BRAIN-ICU Study Investigators (2013) Long-term cognitive impairment after critical illness. *N Engl J Med* 369:1306–1316. doi:[10.1056/NEJMoa1301372](https://doi.org/10.1056/NEJMoa1301372)
28. Iwashyna TJ, Ely EW, Smith DM, Langa KM (2010) Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA* 304:1787–1794. doi:[10.1001/jama.2010.1553](https://doi.org/10.1001/jama.2010.1553)
29. Heyland DK, Garland A, Bagshaw SM, Cook D, Rockwood K, Stelfox HT et al (2015) Recovery after critical illness in patients aged 80 years or older: a multi-center prospective observational cohort study. *Intensive Care Med* 41:1911–1920. doi:[10.1007/s00134-015-4028-2](https://doi.org/10.1007/s00134-015-4028-2)
30. Hofhuis JGM, van Stel HF, Schrijvers AJP, Rommes JH, Spronk PE (2011) Changes of health-related quality of life in critically ill octogenarians: a follow-up study. *Chest* 140(6):1473–1483. doi:[10.1378/chest.10-0803](https://doi.org/10.1378/chest.10-0803)
31. Griffiths J, Hatch RA, Bishop J, Morgan K, Jenkinson C, Cuthbertson BH, Brett SJ (2013) An exploration of social and economic outcome and associated health-related quality of life after critical illness in general intensive care unit survivors: a 12-month follow-up study. *Crit Care* 17:R100. doi:[10.1186/cc12745](https://doi.org/10.1186/cc12745)
32. Kaarlola A, Tallgren M, Pettila V (2006) Long-term survival, quality of life, and quality-adjusted life-years among critically ill elderly patients. *Crit Care Med* 34:2120–2126. doi:[10.1097/01.CCM.0000227656.31911.2E](https://doi.org/10.1097/01.CCM.0000227656.31911.2E)
33. Hoffman KR, Loong B, Haren FV (2016) Very old patients urgently referred to the intensive care unit: long-term outcomes for admitted and declined patients. *Crit Care Resusc* 18:157–164
34. Garrouste-Orgeas M, Timsit JF, Montuclard L, Colvez A, Gattoliat O, Philippart F, Rigal G, Misset B, Carlet J (2006) Decision-making process, outcome, and 1-year quality of life of octogenarians referred for intensive care unit admission. *Intensive Care Med* 32:1045–1051. doi:[10.1007/s00134-006-0169-7](https://doi.org/10.1007/s00134-006-0169-7)
35. Boumendil A, Somme D, Garrouste-Orgeas M, Guidet B (2007) Should elderly patients be admitted to the intensive care unit? *Intensive Care Med* 33:1252–1262. doi:[10.1007/s00134-007-0621-3](https://doi.org/10.1007/s00134-007-0621-3)
36. Luna CM, Palma I, Niederman MS, Membriani E, Giovini V, Wiemken TL et al (2016) The impact of age and comorbidities on the mortality of patients of different age groups admitted with community-acquired pneumonia. *Ann Am Thorac Soc* 13:1519–1526. doi:[10.1513/AnnalsATS.201512-848OC](https://doi.org/10.1513/AnnalsATS.201512-848OC)
37. Le Guen J, Boumendil A, Guidet B, Corvol A, Saint-Jean O, Somme D (2016) Are elderly patients' opinions sought before admission to an intensive care unit? Results of the ICE-CUB study. *Age Ageing* 45:303–309. doi:[10.1093/ageing/afv191](https://doi.org/10.1093/ageing/afv191)
38. Hofmann JC, Wenger NS, Davis RB, Teno J, Connors AF Jr, Desbiens N, Lynn J, Phillips RS (1997) Patient preferences for communication with physicians about end-of-life decisions. SUPPORT Investigators. Study to understand prognoses and preference for outcomes and risks of treatment. *Ann Intern Med* 127:1–12
39. Cohen S, Sprung C, Sjøkvist P, Lippert A, Ricou B, Baras M, Hovilehto S, Maia P, Phelan D, Reinhart K, Werdan K, Bulow HH, Woodcock T (2005) Communication of end-of-life decisions in European intensive care units. *Intensive Care Med* 31:1215–1221. doi:[10.1007/s00134-005-2742-x](https://doi.org/10.1007/s00134-005-2742-x)
40. Lesieur O, Leloup M, Gonzalez F, Mamzer MF, EPILAT study group (2015) Withholding or withdrawal of treatment under French rules: a study performed in 43 intensive care units. *Ann Intensive Care* 5:56. doi:[10.1186/s13613-015-0056-x](https://doi.org/10.1186/s13613-015-0056-x)
41. Heyland DK, Dodek P, Mehta S, Cook D, Garland A, Stelfox HT, Bagshaw SM, Kutsogiannis DJ, Burns K, Muscedere J, Turgeon AF, Fowler R, Jiang X, Day AG, Canadian Critical Care Trials Group and Canadian Researchers at End of Life Network (CARENET) (2015) Admission of the very elderly to the intensive care unit: family members' perspectives on clinical decision-making from a multicentre cohort study. *Palliat Med* 29:324–335. doi:[10.1177/0269216314566060](https://doi.org/10.1177/0269216314566060)
42. Kim J, Choi SM, Park YS, Lee CH, Lee SM, Yim JJ, Yoo CG, Kim YW, Han SK, Lee J (2016) Factors influencing the initiation of intensive care in elderly patients and their families: a retrospective cohort study. *Palliat Med* 30:789–799. doi:[10.1177/02692163166342](https://doi.org/10.1177/02692163166342)

43. Philippart F, Vesin A, Bruel C, Kpodji A, Durand-Gasselín B, Garçon P, Levy-Soussan M, Jagot JL, Calvo-Verjat N, Timsit JF, Misset B, Garrouste-Orgeas M (2013) The ETHICA study (part I): elderly's thoughts about intensive care unit admission for life-sustaining treatments. *Intensive Care Med* 39:1565–1573. doi:[10.1007/s00134-013-2976-y](https://doi.org/10.1007/s00134-013-2976-y)
44. Fuchs L, Novack V, McLennan S, Celi LA, Baumfeld Y, Park S, Howell MD, Talmor DS (2014) Trends in severity of illness on ICU admission and mortality among the elderly. *PLoS One* 9(4):e93234. doi:[10.1371/journal.pone.0093234](https://doi.org/10.1371/journal.pone.0093234)
45. Sznajder M, Aegerter Ph, Launois R, Merlière Y, Guidet B, CubRéa (2001) A cost-effectiveness approach of stays in intensive care units. *Intensive Care Med* 27:146–153
46. Laake JH, Dybwik K, Flaatten HK, Fonneland I-L, Kvåle R, Strand K (2010) Impact of the post-World War II generation on intensive care needs in Norway. *Acta Anaesthesiol Scand* 54:479–484. doi:[10.1111/j.1399-6576.2009.02170.x](https://doi.org/10.1111/j.1399-6576.2009.02170.x)
47. Moreno RP, Metnitz PGH, Almeida E, Jordan B, Bauer P, Campos RA et al (2005) SAPS 3—from evaluation of the patient to evaluation of the intensive care unit. Part 2: development of a prognostic model for hospital mortality at ICU admission. *Intensive Care Med* 31:1345–1355. doi:[10.1007/s00134-005-2763-5](https://doi.org/10.1007/s00134-005-2763-5)
48. Miranda DR, Ryan DW, Schaufeli WB, Fidler V (1998) Organisation and management of intensive care : a prospective study in 12 European countries. <http://public.eblib.com/choice/publicfullrecord.aspx?p=3093836>. Accessed 1 Dec 2016
49. Zampieri FG, Bozza FA, Moralez GM, Mazza DDS, Scotti AV, Santino MS et al (2017) The effects of performance status one week before hospital admission on the outcomes of critically ill patients. *Intensive Care Med* 43:39–47. doi:[10.1007/s00134-016-4563-5](https://doi.org/10.1007/s00134-016-4563-5)
50. Ball IM, Bagshaw SM, Burns KE, Cook DJ, Day AG, Dodek PM, Kutsogiannis DJ, Mehta S, Muscedere JG, Stelfox HT, Turgeon AF, Wells GA, Stiell IG (2016) A clinical prediction tool for hospital mortality in critically ill elderly patients. *J Crit Care* 35:206–212. doi:[10.1016/j.jcrc.2016.05.026](https://doi.org/10.1016/j.jcrc.2016.05.026)
51. Andersen FH, Flaatten H, Klepstad P, Follestad T, Strand K, Krüger AJ, Hahn M, Buskop C, Rime AK, Kvåle R (2016) Long-term outcomes after ICU admission triage in octogenarians. *Crit Care Med* doi:[10.1097/CCM.0000000000002098](https://doi.org/10.1097/CCM.0000000000002098)
52. Cameron JI, Chu LM, Matte A et al (2016) One-year outcomes in caregivers of critically ill patients. *N Engl J Med* 374:1831–1841. doi:[10.1056/NEJMoa1511160](https://doi.org/10.1056/NEJMoa1511160)
53. Azoulay E, Pochard F, Kentish-Barnes N et al (2005) Risk of post-traumatic stress symptoms in family members of intensive care unit patients. *Am J Respir Crit Care Med* 71:987–994. doi:[10.1164/rccm.200409-1295OC](https://doi.org/10.1164/rccm.200409-1295OC)
54. Davis DH, Muniz Terrera G, Keage H et al (2012) Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study. *Brain* 135:2809–2816. doi:[10.1093/brain/aws190](https://doi.org/10.1093/brain/aws190)
55. Wolters AE, van Dijk D, Pasma W et al (2014) Long-term outcome of delirium during intensive care unit stay in survivors of critical illness: a prospective cohort study. *Crit Care* 18:R125. doi:[10.1186/cc13929](https://doi.org/10.1186/cc13929)
56. Docherty AB, Anderson NH, Walsh TS, Lone NI (2016) Equity of access to critical care among elderly patients in Scotland: a national cohort study. *Crit Care Med* 44(1):3–13. doi:[10.1097/CCM.0000000000001377](https://doi.org/10.1097/CCM.0000000000001377)
57. Haas LEM, Karakus A, Holman R, Cihangir S, Reidinga AC, de Keizer NF (2015) Trends in hospital and intensive care admissions in the Netherlands attributable to the very elderly in an ageing population. *Crit Care* 19:353. doi:[10.1186/s13054-015-1061-z](https://doi.org/10.1186/s13054-015-1061-z)
58. Nielsson MS, Christiansen CF, Johansen MB, Rasmussen BS, Tønnesen E, Nørgaard M (2014) Mortality in elderly ICU patients: a cohort study. *Acta Anaesthesiol Scand* 58(1):19–26. doi:[10.1111/aas.12211](https://doi.org/10.1111/aas.12211)
59. Ihra GC, Lehberger J, Hochrieser H, Bauer P, Schmutz R, Metnitz B et al. (2012) Development of demographics and outcome of very old critically ill patients admitted to intensive care units. *Intensive Care Med* 38(4):620–626. doi:[10.1007/s00134-012-2474-7](https://doi.org/10.1007/s00134-012-2474-7)